

### ABSTRACT OF THE DISCLOSURE

A method of screening a substance of interest for heme independent modulation of enzymatic activity of soluble guanylyl cyclase (sGC) is disclosed, comprising (a) obtaining  $\alpha\beta^{\text{Cys105}}$  mutant sGC enzyme; (b) determining activity of the mutant enzyme for forming cGMP from GTP in the presence of the substance of interest in a reaction medium; (c) determining activity as in step (b), except in the absence of the substance of interest; optionally, (d) including an activator other than the substance of interest in steps b) and c); e) comparing results of (b) – (d) to yield a comparison result; and f) from that value of that result, assessing activity of the substance of interest for modulating cGMP production by the mutant enzyme. Increased or decreased formation of cGMP in the presence of the substance of interest indicates activity of the substance for modulating heme independent cGMP production.